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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CLOW, LORI A	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,580	SZALMA ET AL.	
	Examiner	Art Unit	
	Lori A. Clow, Ph.D.	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/22/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments, filed 11 February 2004, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claims 13-16 are currently pending.

The rejections under 35 USC 101 have been withdrawn.

The rejection under 35 USC 112, 2nd paragraph has been withdrawn.

Oath/Declaration

It is acknowledged that Applicant attempted to send a new copy of the declaration, as requested by the Examiner in the previous Office Action. However, the declaration has not been received and the Examiner kindly requests another copy.

Information Disclosure Statement

The Information Disclosure Statement filed 22 January 2002 has not been considered because references 1-4 have not been received. Please re-submit the documents for consideration.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-16 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must be able to select a target protein and retrieve a fingerprint to compare with other generated fingerprints for proteins that represent an entire genome and identify said potential target protein as a target protein for pharmaceutical intervention. For the reasons discussed below, this constitutes undue experimentation.

b) and d) The specification provides no direction on what ligands and proteins should be used in said invention. Further, the specification is devoid of information on exactly what steps to take to generate a fingerprint such that the fingerprint may be compared and contrasted to another fingerprint from a different protein. A fingerprint apparently is a set of values representative of the binding strengths of the different proteins, however, there is no guidance on

the parameters for obtaining such information. In pharmacophore analysis and lead generation, it is known that various descriptors are utilized to characterize molecules. However, the instant specification provides no exact details on just what the fingerprint values consist of and how they are generated. The specification states that the "protein/ligand interaction comparisons comprise identifying the nature of the ligand interaction with each protein in the comparison. Typically the protein/ligand interaction is characterized by a bonding affinity between each protein and each ligand. This could be binary or it could be a numerical variable, such as an equilibrium binding constant or a binding energy (page 7, beginning line20)". Without guidance on the specific generation of the binding constant or the binding energy or perhaps some other variable that would represent a fingerprint, the present invention is not enabled. The specification at page 7 describes an interaction between four ligands and five proteins, which are not named. The nature of the interaction is characterized by bonding affinities and protein annotations are made based upon the interaction assessment and a pattern is established unique to a certain protein. It is unclear from these steps how one would get to step (f) from steps (a)-(e) in the instant claims. How does the protein fingerprint tell anything pertinent to a target for pharmaceutical intervention? There are no parameters that indicate what the binding affinity values mean in terms of pharmaceutical intervention. For instance, is binding a positive indicator or a negative indicator? Are degrees of binding assessed? What is the correlation between the fingerprint and a disease, for instance?

c) The specification provides no working examples of the said method.

e) and g) It would have been well known in the art that descriptors function to characterize molecules so that they may be compared to identify potential drug candidates. The

research in this field is quite extensive and there are several computational programs that implement comparisons of descriptors in order to characterize biological activity. However, absent the guidance on how exactly to perform the broad steps of this invention, one of skill in the art would not have sufficient teaching in order to retrieve and interaction fingerprint and compare it with another for the several thousand proteins in the human genome, for example.

The prior art, for instance, teaches that methods to describe the similarities of molecules have gained increasing interest in rational drug design. Beyond database searching there are many applications of similarity metrics. There are numerous ways to assess the similarity of molecules, **depending on the choice of molecular properties** to compare (Briem et al. J. Med. Chem. (1996) Vol. 39, pages 3401-3408). Briem et al. go on to describe their particular method to compare molecules, known as a DOCK-generated fingerprint method. As is quite clear in this method, the steps are detailed in terms of the generation of the fingerprints and similarity indices (see page 3402 and 3403 formulas). However, the instant specification does not provide the details in such a way that one of skill in the art would know what formulas to use, what databases to use, how to fit them together or distinguish them from any other protein comparison method that exists in the prior art. The generic nature of the specification does not enable one to practice the methods steps of the instant claims.

f) The skill of those in the art of bioinformatics and pharmacogenomics is high.

h) The claims are broad because they are drawn to a method of generating a fingerprint with no further instructions. The skilled practitioner would first turn to the instant specification for guidance to practice methods of generating fingerprints. However, the instant specification does not provide specific guidance to practice these embodiments. As such, the skilled

practitioner would turn to the prior art for such guidance however the prior art shows that there are numerous methods based upon protein interactions.

For the reasons set forth above it would require undue experimentation for one of skill in the art to practice the claimed invention therefore the claims are not enabled.

Response to Applicant's Arguments

Applicant argues that the instant application enables one to collect binding affinity data to generate an interaction fingerprint. While the specification does enable the generation of an interaction fingerprint by creating vectors, there is nothing in the specification that enables the identification of a target protein for pharmaceutical intervention because there are no parameters set forth as to the meaning of the fingerprints in terms of disease. As stated above, what does a fingerprint of a protein tell one about the proteins potential as a candidate for pharmaceutical intervention? What do repeated comparisons have to do with identification of a potential protein target?

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless – (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 16 is rejected under 35 U.S.C. 102(a) as being anticipated by Xenarios et al. (Nucleic Acids Research (2000) Vol. 28, pages 289-291).

Claim 16 is directed toward a computer-implemented system for biological research which comprises a database with gene sequences and interaction fingerprints and a search and computation engine to retrieve and compare fingerprints.

Xenarios et al. teach a database of interacting proteins called DIP. The database is a relational database with protein information including sequence information and protein interactions (page 289, column 2). DIP can be searched in a variety of ways, for instance searching for interactions of a specific protein. Multiple fields can be searched simultaneously to narrow the query (page 290, columns 1 and 2). Each DIP entry reports information about interacting proteins, protein domains, range of proteins involved, interaction, and corresponding experiments, meeting the limitations of claim 16 (page 291, column 1).

No claims are allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242, or (703) 308-4028.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lori A. Clow, Ph.D., whose telephone number is (571) 272-0715. The examiner can normally be reached on Monday-Friday from 10 am to 6:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael P. Woodward, Ph.D., can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Legal Instrument Examiner, Tina Plunkett, whose telephone number is (703) 305-3524, or to the Technical Center receptionist whose telephone number is (571) 272-0549.

MARJORIE MORAN
PATENT EXAMINER
Marjorie A. Moran
5/13/04

May 7, 2004

Lori A. Clow, Ph.D.
Art Unit 1631
Lori A. Clow